

IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

Claims 1-5 (canceled)

6. (currently amended) An isolated polynucleotide comprising:

- (a) the nucleic acid sequence of SEQ ID NO:5;
- (b) a nucleic acid sequence having at least 80% identity to SEQ ID NO:5 and encoding a polypeptide which is a transferase obtainable from a bacterium of the family *Mycobacteriaceae* using adenosyl-GDP-cobamide as substrate and being involved in biosynthesis of vitamin B12, which acts as an aryl transferase or has an activity within EC 2.7.8., and
 - [[(1)]] ~~has an amino acid sequence of SEQ ID NO:6; or~~
 - [[(2)]] ~~is a variant of (1) having at least 70%, 75%, 80%, 85%, at least 90%, at least 95% sequence identity to the amino acid sequence of SEQ ID NO:6;~~
 - or
 - [[(3)]] ~~is a fragment of (1) or (2), which is at least 150 amino acids in length;~~
- (c) a nucleic acid sequence encoding the polypeptide of SEQ ID NO:6 which is complementary to, or which hybridises to, a sequence as defined in (a) or (b);
- (d) a nucleic acid fragment of a sequence which hybridizes under high stringency conditions including hybridization in 0.3 M sodium chloride and 0.03 M sodium citrate at 60°C to a sequence as defined in (a), (b), or (c); or
- (e) ~~a sequence having at least 60% identity to a sequence as defined in (a), (b), (c), or (d); or~~
- [[(f)]] a sequence that is degenerate as a result of the genetic code to any one of the sequences as defined in (a) to (d) [[(e)]].

7. (currently amended) The polynucleotide according to claim 6 wherein ~~in (b) the hybridisation is under stringent conditions, the fragment in (d) is at least 20 nucleotides in length or up to 100, 150, 200 or 300 nucleotides in length or 5 or 10 nucleotides short~~

~~of the coding sequence of SEQ ID NO:5 and/or the identity in (b) [(e)] is at least 70% or 80%, at least 90% or 95%.~~

8. (currently amended) The polynucleotide according to claim 6 which comprises:

- (a) a sequence that encodes a polypeptide having synthase or transferase activity, which is:
 - (1) the coding sequence of SEQ ID NO:5;
 - (2) a sequence which hybridizes under high stringency conditions including hybridization in 0.3 M sodium chloride and 0.03 M sodium citrate at 60°C ~~hybridises selectively~~ to the complement of sequence defined in (1); or
 - (3) a sequence that is degenerate as a result of the genetic code with respect to a sequence defined in (1) or (2); or
- (b) a sequence complementary to a polynucleotide defined in (a).

9. (previously presented) The polynucleotide according to claim 6 which is a DNA sequence.

10. (previously presented) A vector comprising one or more polynucleotide sequence(s) according to claim 6.

11. (previously presented) The vector according to claim 10 which is an expression vector.

12. (currently amended) An isolated [[A]] host cell which comprises at least one polynucleotide according to claim 6, or has multiple copies of one or more of the polynucleotide(s).

13. (currently amended) An isolated [[A]] host cell which comprises, as a heterologous sequence, a polynucleotide according to claim 6.

14. (currently amended) An isolated [[A]] host cell, optionally prokaryotic, transformed with the polynucleotide according to claim 6 or a vector comprising the polynucleotide.

15. (currently amended) A process of producing or synthesizing a polypeptide or vitamin B₁₂ or a precursor thereof, comprising:

- (a) culturing a host cell as defined in claim 12 under conditions that provide for expression of the polypeptide or synthesis of vitamin B₁₂ or a [[the]] precursor thereof and
- (b) isolating said polypeptide or said vitamin B₁₂ or said precursor thereof.

Claims 16-26 (withdrawn)

27. (withdrawn) A process for producing vitamin B₁₂ or a precursor thereof, the process comprising culturing or fermenting a host cell according to claim 12 under conditions such that vitamin B₁₂ or the precursor is produced or synthesised.

Claim 28 (canceled)

29. (withdrawn/currently amended) The vector according to claim 10 comprising which further comprises:

- (a) a polynucleotide encoding a polypeptide wherein said polypeptide ~~acts as a (phospho)transferase or a (nucleotidyl)transferase or has an activity within EC 2.7.1. or EC 2.7.7. or~~ has [[is]] the amino acid sequence of SEQ ID NO:4 or a variant of said SEQ ID NO:4 or a fragment of said SEQ ID NO:4 or has at least 70%, 75%, 80% or 85%, 90%, or 95% identity to the amino acid sequence of SEQ ID NO:4, or the nucleic acid sequence SEQ ID NO:3; and
- (b) a polynucleotide encoding a polypeptide wherein said polypeptide ~~acts as an (aryl)transferase or has an activity within EC 2.7.8. or~~ has it is the amino acid sequence of SEQ ID NO:6 or a variant of said SEQ ID NO:6 or a fragment of said SEQ ID NO:6 or has at least 70%, 75%, 80% or 85%, 90% or 95% identity to the

amino acid sequence of SEQ ID NO:6, or the nucleic acid sequence SEQ ID NO:5.

30. (withdrawn/currently amended) The vector according to claim 10 further comprising a nucleic acid sequence encoding a [[the]] CobA protein.

Claims 31-32 (canceled)

33. (withdrawn) The vector according to claim 11 wherein the polynucleotide is a DNA sequence operably linked to a regulatory sequence.

34. (withdrawn) A process for the preparation of an amine, comprising contacting a substrate with a host cell as defined in claim 12.

35. (withdrawn) A process for the preparation of a phosphate-containing compound, comprising contacting a substrate with a host cell as defined in claim 12.

36. (withdrawn) A process for the preparation of a nucleotidyl-containing compound, comprising contacting a substrate with a host cell as defined in claim 12.

37. (withdrawn) A process for the preparation of an aryl-containing compound, comprising contacting a substrate with a host cell as defined in claim 12.

38. (withdrawn) A process for the preparation of an adenosine-containing compound, comprising contacting a substrate with a host cell as defined in claim 12.

39. (withdrawn) The process of claim 26 wherein the nucleosyl (tri)phosphate is ATP and the transition series metal is cobalt.

40. (withdrawn/currently amended) The vector according to claim 10 ~~comprising which~~ further comprises:

- (a) a polynucleotide encoding a polypeptide wherein said polypeptide ~~acts as a~~ (phospho)transferase or a (nucleotidyl)transferase or has an activity within EC 2.7.1. ~~or EC 2.7.7. or has~~ [[is]] the amino acid sequence of SEQ ID NO:4 or a variant of said SEQ ID NO:4 or a fragment of said SEQ ID NO:4 or has at least 70%, 75%, 80% ~~or 85%, 90% or 95%~~ identity to the amino acid sequence of SEQ ID NO:4, or the nucleic acid sequence SEQ ID NO:3; and
- (b) a polynucleotide encoding a polypeptide wherein said polypeptide ~~acts as an~~ (aryl)transferase or has an activity within EC 2.7.8. ~~or has~~ it is the amino acid sequence of SEQ ID NO:6 or a variant of said SEQ ID NO:6 or a fragment of said SEQ ID NO:6 or has at least 70%, 75%, 80% ~~or 85%, 90% or 95%~~ identity to the amino acid sequence of SEQ ID NO:6, or the nucleic acid sequence SEQ ID NO:5 and further comprising a nucleic acid sequence encoding the CobA protein.

Claim 41 (canceled)

42. (currently amended) The polynucleotide according to claim 6 which further comprises:

- (a) the nucleic acid sequence of SEQ ID NO:3;
- (b) a nucleic acid sequence having at least 80% identity to SEQ ID NO:3 and encoding a polypeptide ~~which is a transferase obtainable from a bacterium of the family *Mycobacteriaceae* using adenosyl cobamide and/or adenosyl cobamide phosphate as substrate and being involved in biosynthesis of vitamin B12, which~~ acts as a nucleotidyl or phospho-transferase or has an activity within EC 2.7.1., EC 2.7.7., and
[[(1)]] ~~has an amino acid sequence of SEQ ID NO:4; or~~
[[(2)]] ~~is a variant of (1) having at least 70%, 75%, 80%, 85%, at least 90%, at least 95% sequence identity to the amino acid sequence of SEQ ID NO:4;~~
or

- [[(3)]] ~~is a fragment of (1) or (2), preferably which is at least 150 amino acids in length;~~
- (c) a nucleic acid sequence encoding the polypeptide of SEQ ID NO:4 ~~which is complementary to, or which hybridizes to, a sequence as defined in (a) or (b);~~
- (d) a nucleic acid fragment of a sequence which hybridizes under high stringency conditions including hybridization in 0.3 M sodium chloride and 0.03 M sodium citrate at 60°C to a sequence as defined in (a), (b), or (c); or
- (e) ~~a sequence having at least 60% identity to a sequence as defined in (a), (b), (c), or (d); or~~
- [[(f)]] a sequence that is degenerate as a result of the genetic code to any one of the sequences as defined in (a) to (d) ~~[(e)]~~.

43. (currently amended) A vector comprising one or more polynucleotide sequence(s) according to claim 42 and wherein the vector optionally further comprises a nucleic acid sequence encoding a CobA protein, ~~wherein the CobA protein is preferably derived from *Propionibacterium freudenreichii*.~~

44. (currently amended) An isolated [[A]] host cell which comprises at least one polynucleotide according to claim 42 or has multiple copies of one or more of the polynucleotide(s).

45. (currently amended) An isolated [[A]] host cell, optionally prokaryotic, transformed with a vector according to claim 43.

46. (currently amended) A process of producing or synthesizing a polypeptide or vitamin B₁₂ or a precursor thereof, comprising:

- (a) culturing a host cell as defined in claim 45 under conditions that provide for expression of the polypeptide or synthesis of vitamin B₁₂ or a precursor thereof and
- (b) isolating said polypeptide or said vitamin B₁₂ or said precursor thereof.

47. (new) The polynucleotide according to claim 42 wherein the identity in (b) is at least 95%.

48. (new) The isolated polynucleotide according to claim 6 encoding a polypeptide having cobalamin (5'-phosphate) synthase activity [EC 2.7.8.-].

49. (new) The polynucleotide according to claim 42 wherein the further comprised polypeptide has cobinamide kinase activity [EC 2.7.1.-] and/or cobinamide phosphate guanyl transferase activity [EC 2.7.7.-].

50. (new) The polynucleotide according to claim 7 which is a DNA sequence.

51. (new) A vector comprising one or more polynucleotide sequence(s) according to claim 7.

52. (new) The vector according to claim 51 which is an expression vector.

53. (new) An isolated host cell which comprises at least one polynucleotide according to claim 7, or has multiple copies of one or more of the polynucleotide(s).

54. (new) An isolated host cell which comprises, as a heterologous sequence, a polynucleotide according to claim 7.

55. (new) An isolated host cell, optionally prokaryotic, transformed with the polynucleotide according to claim 7 or a vector comprising the polynucleotide.

56. (new) A process of producing or synthesizing a polypeptide or vitamin B₁₂ or a precursor thereof, comprising:

- (a) culturing a host cell as defined in claim 53 under conditions that provide for expression of the polypeptide or synthesis of vitamin B₁₂ or a precursor thereof and
- (b) isolating said polypeptide or said vitamin B₁₂ or said precursor thereof.

57. (new) A process for producing vitamin B₁₂ or a precursor thereof, the process comprising culturing or fermenting a host cell according to claim 53 under conditions such that vitamin B₁₂ or the precursor is produced or synthesized.

58. (new) The vector according to claim 10 which further comprises:

- (a) a polynucleotide encoding a polypeptide wherein said polypeptide has the amino acid sequence of SEQ ID NO:4 or has at least 95% identity to the amino acid sequence of SEQ ID NO:4, or the nucleic acid sequence SEQ ID NO:3; and
- (b) a polynucleotide encoding a polypeptide wherein said polypeptide has the amino acid sequence of SEQ ID NO:6 or has at least 95% identity to the amino acid sequence of SEQ ID NO:6, or the nucleic acid sequence SEQ ID NO:5.

59. (new) The vector according to claim 51 further comprising a nucleic acid sequence encoding a CobA protein.

60. (new) The vector according to claim 52 wherein the polynucleotide is a DNA sequence operably linked to a regulatory sequence.

61. (new) The vector according to claim 51 which further comprises:

- (a) a polynucleotide encoding a polypeptide wherein said polypeptide has the amino acid sequence of SEQ ID NO:4 or has at least 95% identity to the amino acid sequence of SEQ ID NO:4, or the nucleic acid sequence SEQ ID NO:3; and
- (b) a polynucleotide encoding a polypeptide wherein said polypeptide has the amino acid sequence of SEQ ID NO:6 or has at least 95% identity to the amino acid

sequence of SEQ ID NO:6, or the nucleic acid sequence SEQ ID NO:5 and further comprising a nucleic acid sequence encoding the CobA protein.

62. (new) The polynucleotide according to claim 7 which further comprises:

- (a) the nucleic acid sequence of SEQ ID NO:3;
- (b) a nucleic acid sequence having at least 80% identity to SEQ ID NO:3 and encoding a polypeptide obtainable from a bacterium of the family *Mycobacteriaceae* using adenosyl cobamide and/or adenosyl cobamide phosphate as substrate and being involved in biosynthesis of vitamin B₁₂;
- (c) a nucleic acid sequence encoding the polypeptide of SEQ ID NO:4;
- (d) a nucleic acid sequence which hybridizes under high stringency conditions including hybridization in 0.3 M sodium chloride and 0.03 M sodium citrate at 60°C to a sequence as defined in (a), (b), or (c); or
- (e) a sequence that is degenerate as a result of the genetic code to any one of the sequences as defined in (a) to (d).

63. (new) A vector comprising one or more polynucleotide sequence(s) according to claim 62 and wherein the vector optionally further comprises a nucleic acid sequence encoding a CobA protein

64. (new) An isolated host cell which comprises at least one polynucleotide according to claim 62 or has multiple copies of one or more of the polynucleotide(s).

65. (new) An isolated host cell, optionally prokaryotic, transformed with a vector according to claim 63.

66. (new) A process of producing or synthesizing a polypeptide or vitamin B₁₂ or a precursor thereof, comprising:

- (a) culturing a host cell as defined in claim 65 under conditions that provide for expression of the polypeptide or synthesis of vitamin B₁₂ or a precursor thereof and
- (b) isolating said polypeptide or said vitamin B₁₂ or said precursor thereof.